

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 214

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

THEODORE JONES and RODNEY M. RICHARDS,
Junior Party,¹

MAILED

v.

SEP 26 2000

R. BRUCE WALLACE,
Junior Party,²

PAT. & T.M. OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

v.

KEITH C. BACKMAN and CHANG-NING J. WANG,
Senior Party.³

¹Application 08/207,241, filed March 7, 1994. Accorded the benefit of U.S. Serial No. 07/220,108, filed June 24, 1988. Assigned to Amgen Inc.

²Application 07/996,771, filed December 24, 1992. Accorded the benefit of U.S. Serial Nos. 07/870,221, filed April 20, 1992 and 07/178,377, filed April 6, 1988. Assigned to City of Hope, Diarte, CA.

³Application 08/015,076, filed February 8, 1993. Accorded the benefit of U.S. Serial Nos. 07/720,739, filed June 25, 1991 (abandoned), and 07/131,936, filed December 11, 1987 (abandoned). Assigned to Abbott Laboratories.

Interference No. 103,420

Patent Interference No. 103,420

FINAL HEARING: August 23, 2000

Before CAROFF, LORIN, and SPIEGEL, Administrative Patent Judges.
CAROFF, Administrative Patent Judge.

FINAL DECISION (37 CFR § 1.658(a))

Originally, this interference involved four parties. Judgment has already been entered against Segev (Paper No. 165). The remaining parties are Jones et al. (Jones), Wallace and Backman et al. (Backman), each having an application involved in the interference.

According to the record before us, the Jones application is assigned to Amgen Inc.; the Wallace application is assigned to City of Hope; and the Backman application is assigned to Abbott Laboratories.

The subject matter in issue relates to a method of amplifying target nucleic acid in a sample involving repetitive hybridization and joining of two pairs of nucleic acid probes.

This method is more specifically defined by the following count, the sole count in this interference:⁴

A method of amplifying target nucleic acid in a sample comprising the steps of:

(a) providing nucleic acid of the sample as single-stranded nucleic acid;

(b) providing in the sample a stoichiometric excess of at least four nucleic acid probes, wherein: i) the first and second of said probes are primary probes, and the third and fourth of said probes are secondary nucleic acid probes; ii) the first probe is a single strand capable of hybridizing to a first segment of a primary strand of the target nucleic acid; iii) the second probe is a single strand capable of hybridizing to a second segment of said primary strand of the target nucleic acid; iv) the 5' end of the first segment of said primary strand of the target is positioned relative to the 3' end of the second segment of said primary strand of the target to enable joining of the first probe to the second probe, when said probes are hybridized to said primary strand of said target nucleic acid, thus forming a reorganized primary molecule having a first portion and a second portion; v) the third probe is capable of hybridizing to a first portion of the reorganized primary molecule; and vi) the fourth probe is capable of hybridizing to a second portion of the reorganized primary molecule, the first portion of the reorganized primary molecule being positioned relative to the second portion of the reorganized primary molecule to enable joining the third probe to the fourth probe when said third and fourth probes are hybridized to said reorganized primary molecule, thus forming a reorganized secondary molecule, said first, second, third, and fourth probes being provided at concentrations to enable said joining;

(c) repeatedly performing the following cycle:

i) hybridizing said probes with nucleic acid in said sample;

⁴We shall refer to the method defined by the count as a ligase chain reaction, or "LCR."

ii) performing said joining to form said reorganized molecules; and

iii) denaturing nucleic acid in said sample.

The claims of the parties which correspond to this count are:

Jones : Claims 1-39

Wallace : Claims 5-9, 11-17 and 19-28

Backman : Claims 1-2, 4-9, 11-19 and 22-48

Issues

The following matters were raised in the parties' briefs and, therefore, define the only issues before us for consideration:⁵

I. Jones motion to designate its claims 6-18 and 20-39 as not corresponding to the count (Motion 8: dismissed).

II. Wallace motion to amend its claims 5, 12, 14 and add claims 51-52 (Motion 19: deferred to final hearing).

⁵Each of the preliminary motions listed is identified by the numerical designation assigned to it in the Decision on Motions of March 21, 1997 (Paper No. 111), and the disposition of each motion by the Administrative Patent Judge (APJ) is indicated in parentheses.

Preliminary motions and other matters which have not been raised in the briefs are regarded as having been abandoned. See Photis v. Luckenheimer, 225 USPQ 948, 950-51 (Bd. Pat. Int. 1984).

III. Backman motion for judgment that all of Wallace's involved claims are unpatentable under 35 U.S.C. § 102(f) for failure to name Dr. Wu as a co-inventor (Paper No. 168: deferred to final hearing).⁶

IV. Whether evidence adduced by Wallace is sufficient to establish a conception and actual reduction to practice of the method defined by the count prior to Backman's effective filing date of Dec. 11, 1987.⁷

V. Backman motion to suppress evidence and to add the thesis of Dr. Wu to the record (Paper No. 204).

Each of the parties filed briefs and appeared, through counsel, at final hearing. In addition, Wallace and Backman each presented a testimonial record and submitted exhibits.⁸

⁶Subsequent to the Decision on Motions of May 21, 1997 (Paper No. 111), the APJ granted Backman leave to file this additional preliminary motion in Paper No. 164, and consideration of the motion on the merits was deferred to final hearing.

⁷Although both Wallace and Backman indicate in their respective briefs that Backman's effective filing date is Dec. 12, 1987, according to the record before us the correct date appears to be Dec. 11, 1987. In any event, this discrepancy will not affect the outcome of this interference inasmuch as Wallace's proofs are directed to an alleged actual reduction to practice a number of months earlier than either of the dates in question.

⁸The record, exhibits, brief and reply brief of Wallace will be respectively referred to hereinafter by the abbreviations "WR", "WX", "WB" and "WRB" followed by an appropriate page or
(continued...)

No issue of interference-in-fact has been raised in this proceeding.

We shall now address each of the issues before us seriatim.

I. Jones Claims 6-18 and 20-39 (Motion 8)

In Motion 8, Jones moved to designate some of its claims as not corresponding to the count. The motion was originally opposed by Wallace; however, Wallace has not renewed its opposition in either its brief or reply brief. Accordingly, we view the Wallace opposition as having been abandoned.

The motion was dismissed by the APJ in his Decision on Motions of May 21, 1997, and a request for reconsideration was denied on November 20, 1998 (Paper No. 166).

After consideration of the remarks presented in Jones' brief, we agree with Jones that the motion at issue was improperly dismissed and, indeed, should have been granted for the reasons given by Jones.

To wit, we find that the claims at issue include a requirement that each of two detection probes must be complementary to a sequence spanning a ligation junction in an

⁸(...continued)
exhibit number. Similar abbreviations will be used when referring to the Jones brief (JB), and the record, exhibits and brief of Backman (BR, BX, BB).

amplification product which has three or more ligated segments, and must hybridize to the amplification product in a contiguous manner to form a detection product.

As noted by Jones, this requirement places distinct physical limitations on the detection probes such that, inter alia, the length of the detection probes are dependent upon the length of the middle amplification product segment, and ensures that only amplification products having the correct sequence of segments are detected so as to minimize detection of amplification product formed by random, blunt-end ligation. By contrast, no other claims corresponding to the count include such a specific requirement. Moreover, Jones avers that none of the prior art of record in the prosecution histories of any of the applications involved in this interference teach or suggest such a concept. In our view, this is sufficient to establish prima facie, that the claims at issue are directed to a "separate patentable invention" as defined by 37 CFR § 1.601(n).

There is no requirement in the statute or rules that the prior art be addressed in an affidavit by an expert witness, as the APJ seemed to suggest in his Decision on Motions. A party may be able to make the necessary showing under 37 CFR

§ 1.637(c)(4)(ii) by argument alone. See Orikasa v. Oonishi, 10 USPQ2d 1996, 2000 n.12 (Comm'r Pats. & Trademarks 1989).

In view of the foregoing, this interference is being redeclared in a concurrent paper to designate Jones' claims 6-18 and 20-39 as not corresponding to the count.

However, since Jones is a junior party and did not allege any date in its preliminary statement prior to the effective filing date of senior party Backman, judgment against Jones is in order as to its remaining claims 1-5 and 19 corresponding to the count. In this regard, see the Order to Show Cause under 37 CFR § 1.640(d)(3), which was issued in Paper No. 111 (page 14).

II. Wallace Motion to Amend and Add Claims (Motion 19)

The subject motion was filed under 37 CFR § 1.633(i) in response to two motions for judgment by Backman (Motions 9 and 10) attacking the patentability of Wallace's involved claims. Consideration of each of these motions, including Motion 19, was deferred to final hearing provided that the questions raised in the Backman motions for judgment were again presented by Backman in its brief. See the Decision on Motions (Paper No. 111, page 7).

Since Backman has not renewed its motions for judgment in its brief at final hearing, the issues raised in those motions

are considered abandoned. Consequently, we find it unnecessary to consider Wallace's responsive motion, Motion 19. Wallace may choose to raise the matter again before the primary examiner, without prejudice, upon resumption of ex parte prosecution of its involved application after termination of this interference.

III. The Inventorship Issue under 35 U.S.C. § 102(f)

Backman asks us to find Wallace's involved claims unpatentable under 35 U.S.C. § 102(f) for improper inventorship since, according to Backman, Daniel Wu should have been named as a co-inventor with Dr. Wallace (BB-21).

Concerning inventorship, statements in patent applications as to sole or joint invention are prima facie evidence of such fact; and a party, relying upon his application, does not have to prove such facts. Thus, a party who wishes to dispute sole inventorship as stated in the application, as Backman does here, has the burden of overcoming the prima facie affect of the application. See Fritsch v. Lin, 21 USPQ2d 1737, 1739 (Bd. Pat. App. & Int. 1991); 3 Rivise & Caesar, Interference Law and Practice, § 407 (Michie Co. 1947). Stated another way, Backman, as the party challenging the patentability of an opponent's claims by preliminary motion, bears the burden of persuasion on

the issue. See Behr v. Talbott, 27 USPQ2d 1401, 1405 (Bd. Pat. App. & Int. 1992).

There is no dispute that Backman, in order to prevail on the inventorship issue, must show by a preponderance of the evidence that the LCR concept communicated by Dr. Wallace to Wu in 1987 was not complete, and the experimental work conducted by Wu at the behest of Wallace was necessary for a complete conception. The test of complete conception is whether the disclosure by the purported inventor, here Wallace, was such that no extensive research or undue experimentation would be required for one of ordinary skill in the art to reduce the concept to practice based upon that disclosure. See Burroughs Wellcome Co. v. Barr Lab., Inc., 40 F.3d 1223, 1229-30, 32 USPQ2d 1915, 1921 (Fed. Cir. 1994), cert. denied, 515 U.S. 1130 (1995); Vanderkooi v. Hoeschele, 7 USPQ2d 1253, 1255 (Bd Pat. App. & Int. 1987). The standard for complete conception is not essentially different from that required for proving sufficiency of disclosure under 35 U.S.C. § 112. See Spero v. Ringold, 377 F.2d 652, 659-60, 153 USPQ 726, 731-32 (CCPA 1967).

After a thorough evaluation of the evidentiary record in this proceeding in light of the opposing positions taken by the parties in their briefs, we agree with Wallace, essentially for

the reasons presented in its reply brief, that Backman has not established by a preponderance of the evidence that Wu made an inventive contribution to the LCR method conceived by Dr. Wallace. Indeed, we find that the preponderance of the evidence suggests that the work done by Wu in 1987 toward reduction to practice of the LCR concept was of a routine nature and did not involve undue experimentation.

In our view, the following factors in particular, which are discussed at length in Wallace's reply brief, are dispositive:

- The level of ordinary skill in the pertinent art at the time in question was high; a person of ordinary skill typically had a graduate degree in the field and at least one year of post-doctoral experience (WR-81).
- At the time, Wu had considerably less experience and education than a scientist of ordinary skill in the art. As a graduate student, Wu had no prior experience with ligation reactions (WR-41, 83, 152-3).
- Wu consulted the scientific literature prior to starting his experimental work on LCR (WR-44).
- By 1987, the scientific literature had identified the critical variables and conditions affecting the hybridization and ligation reactions upon which the LCR method depends (WR 84-88).

- Blunt-end ligation and the conditions under which it would or would not occur, including its promotion by polyethylene glycol (PEG), were also recognized in the scientific literature prior to 1987 (WR 88-89).

- Wu used a well known technique to distinguish the intended amplification product, produced by template-directed ligation, from unintended blunt-end ligation products, viz., he ran negative controls (WR-50, 90; WX-42, p. 81, samples 1-5).

- Wu successfully performed his Experiment 20, the culmination of his methodical efforts to reduce Dr. Wallace's conception to practice, only about one month after starting his experimental work on the LCR project. To wit, Experiment 1 was begun on May 18, 1987 and the results of Experiment 20 were recorded in Wu's laboratory notebook on June 19, 1987 (WR-45, 46, 50; WX-42).

In a nutshell, it is our opinion that Backman has failed to establish by a preponderance of evidence that the work carried out by Wu was of a non-routine nature or involved undue experimentation. The mere fact that Wu had to determine optimum or effective ranges for basic process parameters (e.g., reaction times, reaction temperatures, probe concentrations, probe lengths, salt conditions, effects of PEG) does not by itself

establish that undue or non-routine experimentation was required to do so. As we have previously noted, there is ample evidence that these parameters were recognized in the art as known to affect the hybridization and ligation reactions which form the basis of the LCR technique conceived by Wallace (WR 84-89). As noted by Wallace (WRB 31-32), Backman's reliance on the testimony of Wu to support a contrary conclusion is unfounded. In each instance in which Wu was asked about the state of the scientific literature, Backman's counsel limited the scope of the inquiry to "ligation-based amplification methods" rather than to the specific individual reactions underlying the LCR technique conceived by Wallace (WR 135-141). Accordingly, we give little weight to the negative responses elicited by such questions.

Further, in our view, the testimony of Dr. Backman (BR 16-31) is insufficient to establish that Wu made an inventive contribution to the LCR concept of Dr. Wallace. In essence, Dr. Backman opines that even if certain individual aspects of ligation reactions were known, the operative process conditions of the LCR method are interrelated and, therefore, must be carefully balanced by creative, empirical design. However, as we have said, the mere fact that Wu had to determine effective ranges for recognized parameters in the particular context of LCR

is not dispositive as to whether undue or non-routine experimentation was involved.

IV. Wallace's Case for Priority

Wallace, being a junior party, has the burden of proving prior inventorship by a preponderance of the evidence. Peeler v. Miller, 535 F.2d 647, 651-52, 190 USPQ 117, 120-21 (CCPA 1976).

Wallace alleges conception and actual reduction to practice of the method defined by the count prior to Backman's effective filing date.⁹ After careful review of the evidentiary record in light of the opposing positions of the parties manifested in their briefs, we conclude that a preponderance of the evidence does indeed establish that Daniel Wu reduced the method at issue to practice at the behest of Wallace in June of 1987, prior to Backman's effective filing date.

We have determined, supra, that Wu's work in reducing the LCR concept to practice did not make Wu a co-inventor of the LCR

⁹The question of Wallace's diligence with respect to an actual or constructive reduction to practice, within the context of 35 U.S.C. § 102(g), does not arise here since the question was not argued in Wallace's brief. Therefore, in order to establish prior inventorship, Wallace must prove to have been the first to reduce the invention at issue to practice regardless of any earlier conception date. Accordingly, any proof of an earlier conception date is not material to Wallace's case; conception being subsumed within any proven reduction to practice which inures to the benefit of Wallace. Cf., Smith v. Bousquet, 111 F.2d 157, 160, 45 USPQ 347, 349-50 (CCPA 1940).

method. Thus, Wu's testimony, taken with the entries he made in his laboratory notebook (WX-42), provide the primary source of corroboration for an actual reduction to practice of Wallace's invention.

At the time in question, Daniel Wu was a graduate student and Dr. Wallace was his Ph.D. thesis advisor (WR-41). Wu conducted a series of experiments in May and June of 1987 as part of his assigned research project relating to the LCR amplification method which had been disclosed to him by Dr. Wallace. Wu documented his work in his laboratory notebook and, from time to time, reviewed the experimental results with Dr. Wallace (WR-45).

Wallace alleges that a reduction to practice of the LCR amplification method is manifested by each of experiments 6 and 20, as recorded in Wu's notebook. While we agree that the record supports Wallace's contention as regards Experiment 20, we cannot say the same for Experiment 6.

As for Experiment 6, we note that the count requires "repeatedly performing" a cycle which includes the joining of both pairs of nucleic acid probes to form "said reorganized molecules." Thus, we agree with Backman (BB 5-7) that a single cycle, according to the count, requires two joining (ligation)

events, each involving the joining of a pair of probes, to form both a "reorganized primary molecule" and a "reorganized secondary molecule." The plain meaning of the count language clearly requires a repetition of this cycle.

As is evident from Wu's testimony (WR 48-49), he apparently uses the term "cycle" in a different context to refer to a single ligation step. In effect, the "two cycles" of Experiment 6, as referred to by Wu, constitute a single cycle as defined by the count. Thus, Experiment 6 did not involve the repeated cycling as called for by the count.

Furthermore, Wu's notebook reports (in connection with the results of Experiment 6) that "[t]his low yield is fatal to the eventual goal of achieving amplification;" thus indicating that Wu had no contemporaneous appreciation of success as regards any amplification of the target nucleic acid at the close of Experiment 6. While there is some testimony to the effect that Wu considered Experiment 6 to be a "successful experiment" (WR-48, 228, 260), this is not the same as saying that Experiment 6 constituted an instance of successful amplification.

By contrast, we find that there is ample evidence to establish that Experiment 20 satisfies each limitation of the count. The evidence shows that Peter Walker (of the City of Hope

DNA Synthesis Laboratory) synthesized oligonucleotide probes in response to a request from Wu (WR-56; WX-41). A pair of probes were designed to hybridize to the target sickle cell template in the manner described by the count (WR-46). A second pair of probes were designed to hybridize to the ligation product of the first pair of probes (WR-48). These probes were used in Experiment 20 which involved five rounds of ligation, with an excess of probes being provided in the presence of sickle cell template (samples 6-10), wild-type template (samples 11-15) and no template (as a control: samples 1-5). The reaction products were applied to a polyacrylamide gel, and bands of increasing intensity representative of exponential accumulation of ligation products were observed. A cut out portion of the autoradiograph was used to quantitatively measure the optical density of the bands, and the efficiency of the amplification was calculated to be 98%, based upon that data. (WR-45, 50, 244-46; WX-42, pp. 81-85).

It is Backman's position that the evidence relating to Experiment 20 does not establish a reduction to practice of the method defined by the count. First of all, according to Backman, there is a discrepancy between the record (WR-50) and Wu's notebook (WX-42, p. 82) as to the naming of the probes. To wit,

the record refers to probes "ON β^s 1-4; whereas the first two probes referred to on page 82 of the notebook are designated as ON β^s 1-1 and ON β^s -2.8. However, this apparent discrepancy is not fatal to Wallace's case. As explained by Wallace (WRB 14-15), Wu apparently used the ".8" designation, rather than an asterisk, to identify the second probe on page 82 of his notebook as an 8-mer (WR-243; WX-42, p. 4). Similarly, use of the "s1" superscript, rather than an "s" superscript, in designating the first probe appears to be nothing more than a minor transcription error since no probe used before or after that entry carried an "s1" designation. Certainly, no other evidence contradicts Wu's testimony to the effect that the first probe was in fact ON β^s -1.

Further, Backman argues that Wallace's case for reduction to practice is deficient because there is no evidence that the alleged amplification product of Experiment 20 was ever analyzed (e.g. sequenced) to determine whether it was in fact the intended amplification product. This argument is unpersuasive for a number of reasons.

First of all, there is evidence in Wu's lab notebook (optical density measurements and calculations), and in his testimony, which is apparently consistent with achieving the desired amplification, and which manifests Wu's conviction of

success that he did indeed succeed in amplifying the target nucleic acid (WX-42, p. 83; WR-50, 245-46).

Second, Wu ran negative controls to distinguish the intended amplification product, produced by template-directed ligation, from unintended blunt-end ligation products (WR-50, 90; WX-42, p. 81, samples 1-5).

Third, the count does not require obtaining any particular amplification product having a specific sequence. The count only requires that a result or signal be obtained which is indicative of amplification. This is to be distinguished from a situation where a count explicitly requires that a product be obtained which has a particular structure or sequence. Cf. Schendel v. Curtis, 83 F.3d 1399, 1402-03, 38 USPQ2d 1743, 1746 (Fed. Cir. 1996).

Thus, there is ample evidence to suggest that the desired amplification was attained by Wu in Experiment 20. There is little in the way of contradictory evidence. Consequently, the party Wallace has satisfied its burden of proof by presenting evidence sufficient to establish that the existence of the contested fact (amplification) is more probable than its nonexistence. Cf. Photis, 225 USPQ at 954.

Additionally, Backman argues that Wallace's case for reduction to practice is deficient because the most relevant portion of the gel autoradiograph (WX-42, p. 85) was cut out and never produced as evidence. This argument is unpersuasive since there appears to be a logical reason to explain why that portion was cut out. To wit, the cut out portion was used to measure the optical density of the bands so that an amplification efficiency could be calculated (WR-50, 245-46). The optical density measurements appear on page 83 of Wu's lab notebook. There is no legal requirement in interference practice that the primary source of data, here the cut out portion of the gel autoradiograph, must be produced. All that is required is evidence, of a testimonial and/or documentary nature, sufficient to establish that the existence of the contested fact (amplification) is more probable than its nonexistence. Id. Here, the evidence shows that Wu obtained optical density measurements from the cut out portion of the gel autoradiograph, and used these measurements to calculate an amplification efficiency. This is sufficient, without any credible evidence to the contrary, to establish that it was more likely than not that Wu was convinced that he did achieve amplification in Experiment

20, and obtained optical density data to demonstrate that fact in quantitative terms.

For all of the foregoing reasons, we find that Wallace prevails on the issue of prior inventorship.

V. Backman's Motion to Suppress

The subject motion consists of two parts. In the first part, Backman moves to suppress a "Genomics" article authored by Wu and Wallace (WX-49), and the second Joyce declaration (WR 92-99). In the second part, Backman moves for leave to add the Wu thesis (BX-20). The second part of the motion is unopposed.

The first part of the motion to suppress is dismissed as moot since our previous remarks should make clear that we have found it unnecessary to consider the "Genomics" article and the second Joyce declaration in reaching our decision in favor of Wallace.

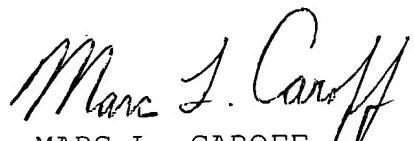
The second part of the motion to suppress, being unopposed, is hereby granted. We have considered Wu's thesis in relation to the inventorship issue, supra, but find that it is not dispositive on that issue. The fact that the thesis may represent original work by Wu does not establish that the work done amounted to an inventive contribution to the LCR concept of Dr. Wallace. Work may be "original" and, yet, not meet the

standard for "inventive contribution." Cf. Fritsch v. Lin,
21 USPQ2d 1731, 1736 (Bd. Pat. App. & Int. 1991).

Judgment.

For the foregoing reasons, judgment as to the subject matter of the sole count in issue is hereby awarded to party Wallace.

Accordingly, Wallace is entitled to a patent containing its involved claims 5-9, 11-17 and 19-28. Party Jones is not entitled to a patent containing its involved claims 1-5 and 19. Senior party Backman is not entitled to a patent containing its involved claims 1-2, 4-9, 11-19 and 22-48.



MARC L. CAROFF)
Administrative Patent Judge)



HUBERT C. LORIN)
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) BOARD OF PATENT
APPEALS AND
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